

SYSTEM AND METHOD OF MOLECULE COUNTING USING FLUCTUATION**ENHANCED SENSORS****Cross-reference to Related Applications**

[0001] This application is a continuation-in-part of commonly-assigned, pending, Non-Provisional Application No. 10/677,684, entitled System and Method of Fluctuation Enhanced Gas-Sensing using SAW devices, filed October 02, 2003, herein incorporated by reference. Application No. 10/677,684 claims the benefit of Provisional Application No. 60/475,058, filed May 30, 2003, also, herein incorporated by reference.

Federally-Sponsored Research and Development

[0002] The SYSTEM AND METHOD OF MOLECULE COUNTING USING FLUCTUATION ENHANCED SENSORS is available for licensing for commercial purposes. Licensing and technical inquiries may be directed to the Office of Patent Counsel, Space and Naval Warfare Systems Center, San Diego, Code 20012, San Diego, CA, 92152; telephone (619)553-3001, facsimile (619)553-3821.

Summary of the Invention

[0003] In one aspect of the invention, a method for analyzing a chemical analyte includes the steps of: (1) generating a fluctuation output signal in response to a plurality of frequency fluctuations in the oscillatory output signal of a surface acoustic wave (SAW) sensor where the fluctuations are responsive to adsorption of molecules on a surface of the SAW sensor; (2) transforming the fluctuation output signal into an amplitude density signal that represents the amplitude density of the frequency fluctuations; and (3) generating an analyte output signal that is representative of a total number of the adsorbed molecules.

[0004] In another aspect of the invention, a chemical sensor system is provided that includes a chemical sensor arranged to produce an oscillatory output signal responsive to adsorption of molecules of a chemical analyte by a primary surface of the sensor. The chemical sensor system also includes: measurement means for measuring a plurality of frequency fluctuations of the oscillatory output signal of the sensor; amplitude density means for generating an amplitude density signal representative of the amplitude density of the frequency fluctuations; and decision means for generating an analyte output signal representative of

1 a total number of the adsorbed molecules in response to the
2 amplitude density signal.

3 **[0005]** In still another aspect of the invention a computer
4 program product (CPP) is provided that includes a machine-
5 readable recording medium and a first, second, and third
6 instruction means recorded on the medium for use with a chemical
7 sensor system that includes a chemical sensor arranged to
8 produce an oscillatory output signal when exposed to a chemical
9 analyte. The first, second, and third instruction means are
10 recorded on the medium for directing the chemical sensor system
11 to: (1) generate a fluctuation output signal in response to a
12 plurality of frequency fluctuations in the oscillatory output
13 signal of the chemical sensor; (2) generate an amplitude density
14 signal representative of the amplitude density of the frequency
15 fluctuations; and (3) generate an analyte output signal that
16 identifies a total number of adsorbed molecules of the analyte.

17 **[0006]** In yet another aspect of the invention, a method for
18 analyzing a chemical analyte includes the steps of: (1)
19 generating a surface acoustic wave across a surface of a
20 structure; (2) transducing the surface acoustic wave into an
21 oscillatory output signal; (3) generating a fluctuation output
22 signal in response to a plurality of frequency fluctuations in
23 the oscillatory output signal, where the fluctuations are

1 responsive to the adsorption of molecules of the chemical
2 analyte on the surface of the structure; (4) generating an
3 amplitude density histogram in response to the fluctuation
4 output signal; and (5) generating an analyte output signal that
5 identifies a total number n of the adsorbed molecules.

Brief description of the Drawings

[0007] FIG. 1 is a block diagram of a chemical sensor system in accordance with the system and method of molecule counting using fluctuation enhanced sensors.

[0008] FIG. 2 is a block diagram of a surface of a chemical sensor in accordance with the system and method of molecule counting using fluctuation enhanced sensors.

[0009] FIG. 3 is a flow-chart of a method in accordance with the system and method of molecule counting using fluctuation enhanced sensors.

[0010] FIG. 4 is a computer program product in accordance with the system and method of molecule counting using fluctuation enhanced sensors.

[0011] FIG. 5 is a view showing theoretical amplitude density histograms in accordance with the system and method of molecule counting using fluctuation enhanced sensors.

[0012] FIG. 6 is a view showing simulated measurements of amplitude density functions in accordance with the system and method of molecule counting using fluctuation enhanced sensors.

Description of Some Embodiments

[0013] Following is a glossary of terms used to describe the system and method for molecule counting using fluctuation enhanced sensors. The definitions set forth in the glossary are representative of the intended meanings as used herein.

GLOSSARY

[0014] The term "amplitude density" $g(U)$ may be mathematically defined as follows: $P(U_0, dU) = g(U) \cdot dU$, where $P(U_0, dU)$ is the probability of finding the amplitude around the amplitude value U_0 in the range of dU width. The amplitude density may be approximated by an amplitude density histogram of the measured time series.

[0015] The term "bandpass filter" means a wave filter that attenuates frequencies on one or both sides of a single transmission band.

[0016] The term "chemical analyte" means a substance being measured in an analytical procedure.

[0017] The term "chemical sensor" means a device that responds to chemical stimulus.

[0018] The term "diffusion coefficient" means a coefficient used to represent the random motion of the molecules on the surface of the SAW device. By way of example, the diffusion

1 coefficient may be represented by: $\langle r^2 \rangle \propto D \cdot t$, where r is the
2 distance traveled by an analyte molecule, D is the diffusion
3 coefficient, t is elapsed time, and where the angle brackets
4 represent the arithmetic mean operation.

5 **[0019]** The term "frequency counter" means an instrument in
6 which frequency is measured by counting the number of cycles
7 occurring during an established time interval.

8 **[0020]** The term "machine-readable recording medium" means a
9 physical material in or on which data may be represented wherein
10 the data can be read by an input unit for storage, processing,
11 or display.

12 **[0021]** FIG. 1 shows a block diagram of a gas-sensing SAW
13 device 102 in a chemical sensor system 100, in accordance with
14 the system and method of molecule counting using fluctuation
15 enhanced sensors. SAW device 102 typically includes two
16 electrode pairs 106 and 108. Although SAW device 102 is shown in
17 FIG. 1 as only having two electrodes, it is recognized that any
18 number of electrode pairs for the generation and measurement of
19 surface propagating waves on a SAW device may be implemented.
20 The space between electrode pairs 106 and 108 is referred to as
21 the gas-sensing region 110 or the "sweetspot". In operation, the
22 extra inertial mass of adsorbed molecules 112 decreases the
23 propagation velocity of a generated surface acoustic wave 101

1 and thus the delay time increases between electrode pairs 106
2 and 108. The propagation velocity of surface acoustic wave 101
3 is inversely proportional to the number of adsorbed molecules
4 112 in the gas-sensing region 110.

5 **[0022]** The gas molecules 112 adsorbed on the surface of SAW
6 device 102 execute a surface diffusion process, which is
7 essentially a random walk over the entire surface of SAW device
8 102. Assuming that SAW device 102 has a thin and substantially
9 uniform coating over the whole surface, the diffusion
10 coefficient D of the adsorbed gas molecules is constant along
11 the entire surface of SAW device 102. Alternatively, the surface
12 of SAW device 102 may include one or more active zones. FIG. 2
13 shows an alternative surface 200 of SAW device 102. Asymmetric
14 surface 200 includes active zone 202 and passive zone 204. Also
15 included on asymmetric surface 200 is diffusion barrier 206 that
16 restricts diffusion to zones 202 and 204.

17 **[0023]** Due to independent random walking of each molecule
18 across the surface of SAW device 102, the instantaneous number
19 $N(t)$ of molecules over gas-sensing region 110 will fluctuate with
20 respect to time. Therefore, chemical sensor system 100 will have
21 fluctuations of the mean oscillation frequency f_{osc} and the
22 instantaneous value $\Delta f_{osc}(t)$ of the frequency deviation from the
23 frequency of the gas-molecule-free case will be proportional to

1 $N(t)$. The dynamical properties of the fluctuations in $N(t)$ and
2 the induced frequency fluctuations $\Delta f_{\text{osc}}(t)$ will be determined by
3 the value of D , the geometry of SAW device 102, the gas-sensing
4 region 110, and the active and passive zones.

5 **[0024]** SAW device 102, in FIG. 1, is not drawn to scale and
6 is shown as having a total length 104a, total width 104b, and
7 gas-sensing region length 104c. The primary surface of SAW
8 device 102 has an area defined by total length 104a and total
9 width 104b. By way of example, SAW device 102 may detect one
10 type of molecule with a characteristic diffusion time constant τ_L
11 that is much shorter than a characteristic adsorption-desorption
12 time constant τ_{ad} . The characteristic diffusion time τ_L may be

13 defined as $\tau_L = \frac{L^2}{D}$, where L is the total length 104a of SAW

14 device 102 and D is the diffusion coefficient of the adsorbed
15 gas molecules 112. The characteristic adsorption-desorption time

16 constant τ_{ad} may be defined as $\tau_{\text{ad}} = \frac{\tau_a \cdot \tau_d}{\tau_a + \tau_d}$, where τ_a is the

17 adsorption time constant and τ_d is the desorption time constant.

18 **[0025]** The probability of a molecule residing in a zone on
19 the surface of SAW device 102 is substantially proportional to
20 the area of the zone in question. The probability density of the
21 molecule distribution is approximately:

$$P(r,n) = \frac{n!}{r!(n-r)!} \cdot p^r \cdot (1-p)^{n-r}, \quad \text{EQ. 1}$$

where n and r are nonnegative integers, $r \leq n$, n represents the total number of molecules on the surface of SAW device 102, r represents the number of molecules on an active zone, and p is represented by: $p = \frac{\mu_{\text{active}}}{\mu_{\text{total}}}$, where μ_{total} is the total area of the surface of the SAW device 102 and μ_{active} is the area of the active zone.

[0026] Chemical sensor system 100 optionally includes a bandpass filter 114, for selecting an oscillatory mode of operation, and amplifier 116 coupled to electrodes 106 and 108.

[0027] Also included in chemical sensor system 100 is measurement means for measuring a plurality of frequency fluctuations in oscillatory output signal 117. FIG. 1 shows an example of measurement means as frequency fluctuation counter 118. There are various ways that frequency fluctuation counter 118 may measure these frequency fluctuations. One such method is heterodyning, that is, nonlinearly mixing the oscillatory output signal with a noiseless oscillator signal with a frequency close to the fluctuating signal frequency. At the output of this mixing, the difference of the two frequencies is identified and the relative fluctuations will increase. Zero crossings may then be counted using short-term measurements. The zero crossing

1 measurements would give the actual frequency, while the mean of
2 these would result in the mean frequency. The frequency
3 fluctuations, using this heterodyning method, are the difference
4 of the actual and the mean frequencies.

5 **[0028]** In the case of an asymmetric surface design, as shown
6 in FIG. 2, the instantaneous amplitude, which is output by
7 frequency counter 118, is: $U_{as}(t) = K \cdot N_A(t)$, where K is a
8 calibration constant and $N_A(t)$ is the instantaneous number of
9 molecules in the active zone.

10 **[0029]** Chemical sensor system 100 also includes amplitude
11 density means for generating an amplitude density signal that is
12 representative of the amplitude density of the frequency
13 fluctuations measured in frequency fluctuation counter 118. FIG.
14 1 shows an example of amplitude density means as statistical
15 analyzer 120. Statistical analyzer 120 may generate the
16 amplitude density signal by way of generating an amplitude
17 density histogram of the measured time series output by
18 frequency fluctuation counter 118. By way of example, FIG. 6
19 (a), (b), or (c) may represent outputs of statistical analyzer
20 120.

21 **[0030]** A decision means for generating an analyte output
22 signal 124, that is representative of a total number n adsorbed
23 molecules of the analyte 112, is also included in chemical

1 sensor system 100. Alternatively, analyte output signal may
2 represent a total number of molecules of the analyte 112 in a
3 designated volume. FIG. 1 shows an example of decision means as
4 pattern recognizer 122. Pattern recognizer correlates patterns
5 in the measured amplitude density signal to a theoretical
6 amplitude density histogram generated with EQ. 1. As an example,
7 pattern recognizer 122 may utilize a look-up table, a neural
8 network, or other processing means.

9 **[0031]** FIG. 3 illustrates a method 300 in accordance with the
10 system and method of molecule counting using fluctuation
11 enhanced sensors. Method 300 utilizes statistical analysis of
12 the dynamics of measured frequency fluctuations of a surface
13 acoustic wave (SAW) device that is arranged to produce an
14 oscillatory output signal when exposed to a chemical analyte.
15 Step 302 includes generating a fluctuation output signal in
16 response to a plurality of frequency fluctuations Δf_{osc} of the
17 oscillatory output signal. There are various methods that may be
18 implemented for the measurement of the frequency fluctuations.
19 One such method is heterodyning, that is nonlinearly mixing the
20 oscillatory output signal with a noiseless oscillator signal
21 with a frequency close to the fluctuating signal frequency. At
22 the output of this mixing, the difference of the two frequencies
23 is identified and the relative fluctuations will increase. Zero

1 crossings may then be counted using short-term measurements. The
2 zero crossing measurements would give the actual frequency,
3 while the mean of these would result in the mean frequency. The
4 frequency fluctuations, using this heterodyning method, are the
5 difference of the actual and the mean frequencies.

6 **[0032]** Step 304 transforms the fluctuation output signal into
7 an amplitude density signal that is representative of the
8 amplitude density. The amplitude density may be described,
9 theoretically, by EQ. 1.

10 **[0033]** Using the measured amplitude density implies strongly
11 enhanced selectivity and sensitivity. One factor contributing to
12 higher sensitivity is the fact that, due to the particular shape
13 of the amplitude density of diffusion processes, the diffusion
14 noise can be easily distinguished from other sensor noise
15 processes, such as adsorption-desorption and thermal noise.

16 **[0034]** The strongly enhanced selectivity also stems from the
17 fact that the amplitude density is a pattern, not a single
18 number. Therefore, the strength and the shape of the amplitude
19 density contains information about the number of gas molecules.

20 **[0035]** Lastly, step 306 generates an analyte output signal
21 that is representative of a total number n adsorbed molecules of
22 the chemical analyte, if the amplitude density signal
23 corresponds to a theoretical amplitude density function. As an

1 example, the characteristic signal may be generated by way of a
2 pattern recognizer, a look-up table, or other processing means.

3 **[0036]** FIG. 4 illustrates a computer program product (CPP)
4 400, in accordance with the system and method of molecule
5 counting using fluctuation enhanced sensors. CPP 400 is for use
6 with a chemical sensor system that includes a chemical sensor
7 arranged to produce an oscillatory output signal when exposed to
8 a chemical analyte. CPP 400 includes a machine-readable
9 recording medium 402 and a first, second, and third instruction
10 means, recorded on the recording medium 402.

11 **[0037]** First instruction means 404 are for directing the
12 chemical sensor system to generate a fluctuation output signal
13 in response to a plurality of frequency fluctuations in the
14 oscillatory output signal generated by the chemical sensor.
15 There are various ways that first instruction means 404 may
16 direct the chemical sensor system to measure these frequency
17 fluctuations. One such method is heterodyning, that is
18 nonlinearly mixing the oscillatory output signal with a
19 noiseless oscillator signal with a frequency close to the
20 fluctuating signal frequency. At the output of this mixing, the
21 difference of the two frequencies is identified and the relative
22 fluctuations will increase. Zero crossings may then be counted
23 using short-term measurements. The zero crossing measurements

1 would give the actual frequency, while the mean of these would
2 result in the mean frequency. The frequency fluctuations, using
3 this heterodyning method, are the difference of the actual and
4 the mean frequencies.

5 **[0038]** Second instruction means 406 are for directing the
6 chemical sensor system to generate an amplitude density signal
7 that is representative of the amplitude density of the frequency
8 fluctuations in the oscillatory output signal. By way of
9 example, second instruction means 406 may direct the chemical
10 sensor system to generate the amplitude density signal through
11 generation of an amplitude density histogram of the measured
12 time series of frequency fluctuations in the instantaneous
13 frequency.

14 **[0039]** Third instruction means 408 are for directing the
15 chemical sensor system to generate an analyte output signal that
16 identifies a total number n molecules of the chemical analyte,
17 if the amplitude density signal corresponds to a theoretical
18 amplitude density function. By way of example, the total number
19 of n molecules may represent the total number of molecules on
20 the surface of the chemical sensor. Alternatively, analyte
21 output signal may represent the total number of molecules in a
22 volume. Also, as an example, third instruction means 408 may

1 utilize a look-up table, a neural network, or other processing
2 means.

3 **[0040]** Optionally included in CPP 400 is a fourth
4 instruction means, recorded on the recording medium 402 for
5 directing the chemical sensor system to correlate patterns in
6 the amplitude density signal to the theoretical density
7 function, as generated by EQ. 1.

8 **[0041]** FIG. 5 illustrates theoretical amplitude density
9 histograms in accordance with the system and method of molecule
10 counting using fluctuation enhanced sensors. The three
11 histograms shown were all generated utilizing EQ.1, where $p=0.5$,
12 and $n=1, 2$, and 5 , respectively.

13 **[0042]** FIG. 6 illustrates simulated measurements of the
14 amplitude density functions in accordance with the system and
15 method of molecule counting using fluctuation enhanced sensors.
16 By way of example, FIG. 6 may show outputs of the statistical
17 analyzer 120, of FIG. 1. These measured amplitude densities
18 could then be compared to the theoretical amplitude density
19 histograms, as shown in FIG. 5, to determine the total number of
20 molecules on the surface of the SAW device.